REMARKS

Claims 36-38, 42-47, 51-54, 56, and 57 are pending in the application. Claims 50, 55 and 35 have been cancelled by this Amendment. New claims 56 and 57 have been added. No new matter is added by this Amendment. Support for the subject matter of the new claims is found at least in the specification at page 6, lines 6-11 and 2-3.

Claims 36, 42-44, 46, 47, and 51-54 have been amended to correct claim dependency and to render the antecedent bases of claim elements more clear.

Rejection Under 35 U.S.C. § 112, second paragraph.

The Examiner has rejected claims 35-38, 42-47 and 50-55 under 35 U.S.C. § 112, second paragraph contending that the claims are indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

The Examiner has asserted that claims 35 and 58 are indefinite for use of the phrases "the structural element (a) of the monomer of the plastics material of the surface," "from monomers containing at least one structural element (a) derived from a carboxylic acid," "capable of," and "stable interaction." These claims have been cancelled and none of the phrases is used in the rewritten version of these claims. Accordingly, it is submitted that the § 112 rejection on these grounds is no longer applicable.

The Examiner asserts that claim 47 is indefinite as it allegedly fails to point out what is included or excluded by the claim composition.

The applicants traverse the rejection.

Claim 47 is a conventional composition claim in which one component of a composition that comprises other ingredients is recited. The component, in this case, is the interactive system as described in claim 56. Since a composition containing only one recited component when used with the "comprising" transition phrase is permissible, it is submitted that this claim is not indefinite under 35 U.S.C. § 112.

In view of the foregoing, it is submitted that the Examiner's rejections under 35 U.S.C. § 112, second paragraph, have been overcome or are inapplicable. Reconsideration and withdrawal of the rejection is requested.

Rejections under 35 U.S.C. § 102(b) and (e).

The Examiner has rejected claims 35, 36, 42, 43, 47, 52, and 55 under 35 U.S.C. § 102(b) asserting that they are anticipated by U.S. Patent No. 4,086,199 of Daniel ("Daniel"). The Examiner contends that Daniel discloses an interactive system that includes "latex polymer" particles that function as biological carriers for protein substances. The particles have a core that is a plastic material comprising alkyl acrylates and methacrylates and a cross linker comprising polyethylene glycol dimethacrylate which gives the polymer particles greater resistance to solvents. According to the Examiner's characterization of Daniel, the latex particles are very stable, chemically and mechanically, at extended periods of time, and remain stable at varying pH levels and temperature. The Examiner contends that biologically active substances, such as proteins, are coupled to or adsorbed into the carrier particles.

The Examiner has rejected claims 35, 36, 42, 44, 47, 50, 51, 52, and 55 under 35 U.S.C. § 102(b) as being "inherently anticipated" by U.S. Patent No. 4,575,539 of DeCrosta ("DeCrosta"). The Examiner argues that DeCrosta discloses a drug delivery system in the form of hydrogel beads that include interpenetrating polymer networks which have superior drug loading and release capacity. DeCrosta, according to the Examiner, discloses a first polymer substrate comprising an acrylic swelling agent, methyl methacrylate or acrylic acid, and a cross linking agent, (poly)ethylene glycol dimethacrylate. According to the Examiner the drug delivery system of DeCrosta permits oral delivery of pharmacologically active substances such as antibiotics for the treatment of bacterial and parasitic infections as well as metabolic diseases. The Examiner contends that DeCrosta inherently discloses all of the elements of the invention as it "reads on the claim." Therefore, the Examiner states "it is maintained that the features recited in the claimed invention, *i.e.*, a stable interaction exists between the surface and the linker which comprises hydrogen bonds and which cannot be reversed by pH in the range of from 2 to 13 or temperatures up to 60° C, are inherently taught by DeCrosta [sic]."

The Examiner has rejected claims 35-38, 42-47, and 50-55 under 35 U.S.C. § 102(e) as being "inherently anticipated" by U.S. Patent No. 5,410,016 of Hubbell, *et al.* ("Hubbell").

The Examiner contends that Hubbell discloses an interactive system comprising photopolymerizable, biodegradable hydrogels used as tissue contacting materials or controlled release carriers. The interactive system of Hubbell, as characterized by the Examiner, has a polymerizable region that comprises dimethacrylates and oligomethacrylates. This

polymerizable region may contain a reactive derivative such as an isocyanate or isothiocyanate. The polyermizable macromer includes a core, an extension on each end, and an end cap, wherein the core includes a hydrophilic polyethylene glycol. The physiologically and pharmacologically active drugs coupled to the composition for controlled delivery include proteins, hormones, enzymes, antibiotics, and carbohydrates such as hyaluronic acid, heparin, and heparin sulfate. The Examiner contends that the claims "read on the disclosure" of Hubbell and states that "it is maintained that the features recited in the claimed invention, *i.e.*, a stable interaction exists between the surface and the linker which comprises hydrogen bonds and which cannot be reversed by pH in the range of 2 to 13 or temperatures up to 60° C, are inherently taught by Hubbell, *et al.* [sic]"

The applicants respectfully traverse each of these rejections.

Daniel

Daniel discloses lattices of polymers that are aqueous dispersions of polymers in particle form. The particle is made up of a "core" which represents 50% to 90% by weight of the particle. The core comprises cross-linked homo- or co-polymers of vinyl monomers, including styrene, methylstyrene, vinyl talulene, ethyl vinyl benzene, or alkyl acrylates. The particles of Daniel also include a "periphery" which is 10% to 50% of the particle and is formed by a vinyl or diene monomer and a monomer containing -CN groups which are copolymerized with the vinyl or diene monomer. The monomer containing the -CN group at the periphery is capable of covalently bonding proteins such that the proteins are fixed and the lattice particle acts as a carrier. Thus, the Daniel device is (1) a vinyl polymer copolymer ("core") polymerized to a (2) monomer containing a -CN group ("periphery"). It is the monomer containing a -CN group that is covalently bonded to the protein.

DeCrosta

DeCrosta teaches a drug delivery system that includes interpenetrating polymer networks. The interpenetrating polymer network is made up of a water swellable first polymer network in the form of hydrogel beads that are interpenetrated by a diffusion rate controlling membrane. The diffusion rate controlling membrane is comprised of a second cross-linked polymer formed of the reaction product of an acrylic swelling agent and a cross-linking agent. The

interpenetrating polymer network of the invention of DeCrosta is a combination of two polymers in network form, at least one of which (the second polymer) is synthesized and/or cross-linked in the immediate presence of the other (the first polymer in the form of hydrogel beads). The hydrogel beads disclosed as suitable for the first polymer are taught as being the hydrogels of U.S. Patent Nos. 4,423,099; 4,224,427; 4,056,496; 4,136,250; 4,379,864. The second interpenetrating polymer is formed from the reaction product of (1) an acrylic swelling agent (which may be acrylic acid, methyl methacrylate, acrylic anhydride, ethylene, vinyl acetate, hydroxyl ethyl acrylate, methacrylate, vinyl pyrrolidone, vinyl chloride, methacrylate acid, acylamide, hydroxyl propylmethacrylate, hydroxyl ethyl methacrylate, and butyl acrylate and (2) a cross-linking agent that is a monomer containing at least two vinyl groups.

Hubbell

Hubbell teaches the hydrogels of polymerized and cross-linked macromers. The hydrogels of Hubbell comprise hydrophilic oligomers having biodegradable monomeric or oligomeric extensions. The biodegradable extensions are terminated on free ends with end capped monomers or oligomers capable of polymerizing and cross-linking. The configuration of the hydrogel tissue contacting material of Hubbell is shown in Figure 1. The water soluble core shown by an unbroken line may be polyethylene glycol. From this water soluble core extend hydrolyzable degradable extensions such as polyglycolides. On these extensions is located an end cap which may be an acrylate and the broken line shows a water soluble hydrolizable portion which may be hyaluronate.

None of the Cited References Discloses the Invention.

None of Daniel, DeCrosta, or Hubbell anticipates the invention as none discloses all elements of the invention either expressly or inherently. Further, in the cases where the Examiner has asserted "anticipation by inherency," she has failed to meet her burden of demonstrating that the inherent claim element necessarily flows from the technology disclosed in the prior art references.

The invention is an interactive system that includes the surface of a plastic material that is one of the recited polymers or copolymers and one of recited polymers and copolymers which contains at least one structural element designated (a) which is an ester group of the acrylate or

vinyl ester polymer; and a linker coupled to a pharmaceutically or physiologically active substance. The linker is a polyalkylene glycol, a polyalkylene imine, a polyalkylene amine, a polyoxazilin or a polyalkylene sulfide and the linker is attached to the structural element (a) by a hydrogen bond which cannot be reversed by pH values in the range of 2 to 13 or temperatures of up to 60° C. The linker is attached to the active substance. The [linker-active substance] conjugate is attached (via the linker) to element (A) by a hydrogen bond.

The Examiner's rejections rely on the premise that because the prior art discloses some or all of the component parts of the claimed interactive system, it necessarily possesses all of the elements inherently. Such conclusion is incorrect as a point of both logic and law. In fact, none of the references teach that the component parts are associated with one another such that a hydrogen bond (having the recited characteristics) exists between structural element (A) and the linker. None of the three references describes "linkers" within the meaning of this term in the present application nor, as a consequence, do they disclose linker active substance linkers coupled to a pharmaceutically or a physiologically active substance wherein the [linker-active substance] composition is attached to structural element (A) by a hydrogen bond that cannot be reversed by pH values in the range of 2 to 13 or temperatures up to 60° C.

The linker of the present claims are, *e.g.* polyalkylene glycol, which contains an -OH group that possess the requisite structure such that it can form the hydrogen bond by which it is attached to structural element (A). The Examiner incorrectly considers that the use of polyethylene glycol dimethacrylate as disclosed in Daniel and DeCrosta is a linker as is used within the meaning of this invention. This compound is a cross-linker for polymers and has only methacrylate end groups which react in a polymerization reaction through their double bond to cross-link a polymer. Polyethylene glycol dimethacrylate does not have a structural element capable of establishing a hydrogen bond. In fact, in both Daniel and DeCrosta the chemistry is such that the polyethylene dimethacrylate is used to cross-link a polymer; it is therefore chemically incapable of forming a bond to an active substance or forming a hydrogen bond to structural element (A), the ester group of the acrylate or vinyl ester polymer. Thus, all elements of the invention are not present in either Daniel or DeCrosta.

In Hubbell, the hydrophilic compound is included in the macromer forming the core of the photopolymerizable, biodegradable hydrogels of the Hubbell composition. For this reason,

the compound no longer possesses its terminal -OH groups; they have been "used up." Therefore, it does not form a hydrogen bond with any other component of Hubbell's hydrogels.

The CDI activated PEG 400 monoacrylate of Example 16 of Hubbell (specifically relied upon by the Examiner) is not a linker within the meaning of the present invention. After the compound is reacted with hyaluronic acid it no longer contains a structural unit capable of forming a hydrogen bond (*e.g.*, an -OH group), but instead contains an acrylate residue, which is used to polymerize the "acrylated hyaluronic acid," as explained in Example 16 to obtain a gel. As is clear from the disclosure of Example 16, the hyaluronic acid is not bound via a linker to a previously made polymer surface having structural element (A) using hydrogen bonds. Moreover, even assuming that the linkage was a hydrogen bond, which it is not, the data in Example 16 demonstrate that the bond is at least reversed at pHs of 2 to 13. The hyaluronic acid is characterized as a "degradable region" in Example 16. The active substance is released according to the teachings of Hubbell under physiological conditions, pH values in the range of 2 to 13. This is another indicator that no hydrogen bond as recited in the claims exists between the linker and structural element (A), as such bond would not degrade under physiological conditions.

For at least these reasons, it is respectfully submitted that none of Daniel, DeCrosta and/or Hubbell anticipates the invention. Reconsideration, withdrawal of the rejections and allowance of the claims at the earliest opportunity is respectfully requested.

CONCLUSION

It is submitted that claims 36-38, 42-47, 51-54, 56 and 57 are fully compliant with 35 U.S.C. § 112. Moreover, the claims are patentable over the cited art. Allowance of all pending claims is earnestly solicited.

Respectfully submitted,

ELKE BUCHA, *et al.*

18 may 2004 By: Kristyne A. Bullock
(Date)

KRISTYNE A. BULLOCK
Registration No. 42,371
AKIN GUMP STRAUSS HAUER & FELD LLP
One Commerce Square
2005 Market Street, Suite 2200
Philadelphia, PA 19103-7013
Telephone: 215-965-1200
Direct Dial: 215-965-1348
Facsimile: 215-965-1210
E-Mail: kbullock@akingump.com

KAB:cmb
7163074

Enclosures
Petition for Extension of Time